

Figure 1

CD95

>sp|P25445|TNR6_HUMAN Tumor necrosis factor receptor superfamily member 6 precursor (FASL receptor) (Apoptosis-mediating surface antigen FAS) (Apo-1 antigen) (CD95) - Homo sapiens (Human).

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1 60
MLGIWTLPL VLTSVARLSS KSVNAQVTDI NSKGLELRKT VTTVETQNL GLHHDGQFCH
61 120
KPCPPGERKA RDCTVNGDEP DCVPCQEGKE YTDKAHFSSK CRRCLCDEG HGLEVEINCT
121 180
RTQNTKCRCK PNFFCNSTVC EHCDPCTKCE HGIIECTLT SNTKCKEES RSNLGLCLL
181 240
LLPIPLIVWV KRKEVQKTCR KHRKENQGS ESPTLNPETV AINLSDVDLS KYITTIAGVM
241 300
TLSQVKGFVR KNGVNEAKID EIKNDNVQDT AEQKVQLLRN WHQLHGKKEA YDTLIKDLKK
301 335
ANLCTLAEKI QTIILKDITS DSENSNFRNE IQSLV
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AA 1-16 Signal peptide (potential)
AA 17-173 extracellular domain (potential)
AA 47-83 CRD1
AA 84-127 CRD2
AA 128-166 CRD3
AA 174-190 transmembrane (potential)
AA 191-335 cytoplasmic (potential)

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Figure 2

IgG1

>sp|P01857|GC1_HUMAN Ig gamma-1 chain C region - Homo sapiens (Human).

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1 60
ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYFPEPVTVS WNSGALTSGV HTFPAVLQSS
61 120
GLYSLSSVVT VPSSSLGTQT YICNVNHKPS NTKVDKKVEP KSCDKTHTCP PCPAPELLGG
121 180
PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA KTKPREEQYN
181 240
STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ VYTLPPSRDE
241 300
LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTTPV LDSDGSFFLY SKLTVDKSRW
301 330
QQGNVFSCSV MHEALHNHYT QKSLSLSPGK
```

AA 99-110 hinge region

AA 111-223 CH2 region

AA 224-330 CH3 region

Variants D239E, L241M

Figure 3A

CD95-Fc (AA 1-172 CD95 and AA 102-330 IgG1)

1

60

120

180

240

300

360

400

MLGIWTLLPL VLTSVARLSS KSVNAQVTDI NSKGLELRKT VTTVETQNL E GLHHDGQFCH
KPCPPGERKA RDCTVNGDEP DCVPCQEGKE YTDKAHFSSK CRRCLCDEG HGLEVEINCT
RTQNTKCRCK PNFFCNSTVC EHCDPCTKCE HGIIKECTLT SNTKCKEEGS RSCDKTHTCP
PCPAPELLGG PSVFLFPPKP KDTLMIS RTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA
KTKPREEQYN STYRVVSVLT VLVHQQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ
VYTLPPSREE MTKNQVSLTCLVKGFYPSDI AVEWESNGQP ENNYKTTTPV LDSDGSSFFLY
SKLTVDKSRW QQGNVFSCSV MHEALHNHYT QKSLSLSPGK

Figure 3B

Example of a preferred CD59-Fc fusion protein with an overlapping amino acid:

CD95 extracellular domain	huIgG1
131 <div>173</div> <div>PNFFCNSTVC EHCDPCTKCE HGIIKECTLT SNTKCKEEGS RSN</div>	99 <div>120</div> <div>EP KSCDKTHTCP PCPAPELLGG</div>
PNFFCNSTVC EHCDPCTKCE HGIIKECTLT SNTKCKEEGS RSCDKTHTCP PCPAPELLGG	

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Figure 4**3. TRAIL-R1**

>sp|O00220|T10A_HUMAN Tumor necrosis factor receptor superfamily member 10A precursor (Death receptor 4) (TNF-related apoptosis-inducing ligand receptor 1) (TRAIL receptor-1) (TRAIL-R1) - Homo sapiens (Human).

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1                                     60
MAPPPARVHL GAFLAVTPNP GSAASGTEAA AATPSKVWGS SAGRIEPRGG GRGALPTSMG
61                                     120
QHGPSARARA GRAPGPRPAR EASPRLRVHK TFKFVVVGVL LQVVPSSAAT IKLHDQSIGT
121                                     180
QQWEHSPLGE LCPPGSHRSE HPGACNRCTE GVGYTNASNN LFACLPCTAC KSDEEERSPC
181                                     240
TTTRNTACQC KPGTFRNDNS AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKESGNGHNI
241                                     300
WVILVVTLVV PLLLVAVLIV CCCIGSGCGG DPKCMDRVCF WRLGLLRGPG AEDNAHNEIL
301                                     360
SNADSLSTFV SEQQMESQEP ADLTGVTVQS PGEAQCLLGP AEAEGSQRRR LLVPANGADP
361                                     420
TETLMLFFDK FANIVPFDSW DQLMRQLDLT KNEIDVVRAG TAGPGDALYA MLMKWVNKTG
421                                     468
RNASIHTLLD ALERMEERHA KEKIQDLLVD SGKFIYLEDG TGSAVSLE

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AA 1-23 Signal peptide (potential)

AA 24-239 extracellular domain (potential)

AA 107-145 CRD1

AA 147-188 CRD2

AA 189-229 CRD3

AA 240-262 transmembrane (potential)

AA 263-468 cytoplasmic (potential)

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Figure 5

Examples of Trail-R1-Fc fusion proteins with overlapping amino acids:

Trail R1 extracellular domain		huIgG1	
201	239	99	120
AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKESGNGHN		EP KSCDKTHTCP PCPAPELLGG	
AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKEP KSCDKTHTCP PCPAPELLGG			
201	239	99	120
AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKESGNGHN		EP KSCDKTHTCP PCPAPELLGG	
AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKSCDKTHTCP PCPAPELLGG			
201	239	99	120
AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKESGNGHN		EP KSCDKTHTCP PCPAPELLGG	
AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKESCDKTHTCP PCPAPELLGG			
201	239	99	120
AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKESGNGHN		EP KSCDKTHTCP PCPAPELLGG	
AEMCRKCSRG CPRGMVKVKD CTPWSDIECV HKESGNGHTCP PCPAPELLGG			

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Figure 6**4. TRAIL-R2 (long)**

>sp|O14763|T10B_HUMAN Tumor necrosis factor receptor superfamily member 10B precursor (Death receptor 5) (TNF-related apoptosis-inducing ligand receptor 2) (TRAIL receptor-2) (TRAIL-R2) - Homo sapiens (Human).

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1                                     60
MEQRGQNAPA ASGARKRHGP GPREARGARP GPRVPKTLVL VVAAVLLLVV AESALITQQD
61                                     120
LAPQQRAAPQ QKRSSPSEGL CPPGHHISED GRDCISCKYG QDYSTHWNDL LFCLRCTRCD
121                                     180
SGEVELSPCT TTRNTVCQCE EGTFREEDSP EMCRKCRTGC PRGMVKVGDC TPWSDIECVH
181                                     240
KESGTKHSGE APAVEETVTS SPGTPASPCS LSGIIIGVTV AAVVLIVAVF VCKSLLWKKV
241                                     300
LPYLGICSG GGGDPERVDR SSQRPGAEDN VLNEIVSIQ PTQVPEQEME VQEPAEPTGV
301                                     360
NMLSPGESEH LLEPAEAERS QRRRLVPAN EGDPTETLRQ CFDDFADLVP FDSWEPLMRK
361                                     420
LGLMDNEIKV AKAEAAGHRD TLYTMLIKWV NKTGRDASVH TLLDALETG ERLAKQKIED
421                                     440
HLLSSGKFMV LEGNADSAMS

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AA 1-55 Signal peptide
 AA 56-210 extracellular domain (potential)
 AA 57-94 CRD1
 AA 97-137 CRD2
 AA 138-178 CRD3
 AA 192-206 TAPE
 AA 211-231 transmembrane (potential)
 AA 232-440 cytoplasmic (potential)

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Figure 7

Examples of Trail-R2(long)-Fc fusion proteins with overlapping amino acids ("repeat" included):

Trail R2 (long) extracellular domain		huIgG1	
171	210	99	120
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPCS		EP KSCDKTHTCP PCPAPELLGG	
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPCS			
Bevorzugte Ausführung (wie in EP 03006949.6 beschrieben)			
171	210	99	120
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASPCS		EP KSCDKTHTCP PCPAPELLGG	
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPAS			
171	210	99	120
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASCS		EP KSCDKTHTCP PCPAPELLGG	
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPAS			
171	210	99	120
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASCS		EP KSCDKTHTCP PCPAPELLGG	
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPAS			
171	210	99	120
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASCS		EP KSCDKTHTCP PCPAPELLGG	
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPAS			
171	210	99	120
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASCS		EP KSCDKTHTCP PCPAPELLGG	
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPAS			
171	210	99	120
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASCS		EP KSCDKTHTCP PCPAPELLGG	
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPAS			
171	210	99	120
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASCS		EP KSCDKTHTCP PCPAPELLGG	
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPAS			
171	210	99	120
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPASCS		EP KSCDKTHTCP PCPAPELLGG	
TPWSDIECVH KESGTKHSGE APAVEETVTS SPGTPAS			

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Figure 9**5. TRAIL-R2 (short)**

>sp|O14763|T10B_HUMAN Tumor necrosis factor receptor superfamily member 10B precursor (Death receptor 5) (TNF-related apoptosis-inducing ligand receptor 2) (TRAIL receptor-2) (TRAIL-R2) - Homo sapiens (Human).

```

1                                     60
MEQRGQONAPA ASGARKRHGP GPREARGARP GPRVPKTLVL VVAAVLLLVS AESALITQOD
61                                     120
LAPQQRAAPQ QKRSSPSEGL CPPGHHISED GRDCISCKYG QDYSTHWNDL LFCLRCTRCD
121                                     180
SGEVELSPCT TTRNTVCQCE EGTFREEDSP EMCRCRTGC PRGMVKVGDC TPWSDIECVH
181                                     240
KESGIIIGVT VAAVVLIVAV FVCKSLLWKK VLPYLKGICS GGGGDPERVD RSSQRPGAED
241                                     300
NVLNEIVSIL OPTQVPEQEM EVQEPAEPTG VNMLSPGESE HLEPAEAER SQRRRLVPA
301                                     360
NEGDPTETLR QCFDDFADLV PFDSWEPLMR KLGLMDNEIK VAKAEAAGHR DTLYTMLIKW
361                                     411
VNKTGRDASV HTLLDALETG GERLAKQKIE DHLLSSGKFM YLEGNADSAM S

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AA 1-55 Signal peptide
 AA 56-184 extracellular domain (potential)
 AA 57-94 CRD1
 AA 97-137 CRD2
 AA 138-178 CRD3
 AA 213-202 transmembrane (potential)
 AA 203-411 cytoplasmic (potential)

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Figure 10

Examples of Trail-R2(short)-Fc fusion proteins with overlapping amino acids:

Trail-R2 (short) extracellular domain	huIgG1
151 184 EMCRKCRTGC PRGMVKGDC TPWSDIECVH KESG	99 120 EP KSCDKTHTCP PCPAPELLGG
EMCRKCRTGC PRGMVKGDC TPWSDIECVH KESG KSCDKTHTCP PCPAPELLGG	
151 184 EMCRKCRTGC PRGMVKGDC TPWSDIECVH KESG	99 120 EP KSCDKTHTCP PCPAPELLGG
EMCRKCRTGC PRGMVKGDC TPWSDIECVH KSCDKTHTCP PCPAPELLGG	
151 184 EMCRKCRTGC PRGMVKGDC TPWSDIECVH KESG	99 120 EP KSCDKTHTCP PCPAPELLGG
EMCRKCRTGC PRGMVKGDC TPWSDIECVH KESG KSCDKTHTCP PCPAPELLGG	
151 184 EMCRKCRTGC PRGMVKGDC TPWSDIECVH KESG	99 120 EP KSCDKTHTCP PCPAPELLGG
EMCRKCRTGC PRGMVKGDC TPWSDIECVH KESG KSCDKTHTCP PCPAPELLGG	
151 184 EMCRKCRTGC PRGMVKGDC TPWSDIECVH KESG	99 120 EP KSCDKTHTCP PCPAPELLGG
EMCRKCRTGC PRGMVKGDC TPWSDIECVH KSCDKTHTCP PCPAPELLGG	

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Figure 11**6. TRAIL-R3**

>sp|O14798|T10C_HUMAN Tumor necrosis factor receptor superfamily member 10C precursor (Decoy receptor 1) (DcR1) (Decoy TRAIL receptor without death domain) (TNF- related apoptosis-inducing ligand receptor 3) (TRAIL receptor-3) (TRAIL-R3) (Trail receptor w

```

1                                     60
MARIPKTLKF VVVIVAVLLP VLAYSATTAR QEEVPQQTVA PQQQRHSFKG EEC PAGSHRS
61                                     120
EHTGACNPCT EGV DYT NASN NEPSCFPCTV CKSDQKHKSS CTMTRDTVCQ CKEGTFRNEN
121                                     180
SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVE TPAAEETMNT SPGTPAPAAE
181                                     240
ETMNTSPGTP APAAEETMTT SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPASSHY
241                                     259
LSCTIVGIIV LIVLLIVFV

```

AA 1-23 Signal peptide

AA 24-236 extracellular domain

AA 29-66 CRD1

AA 69-109 CRD2

AA 110-149 CRD3

AA 162-236 5 x 15 AA tandem tape repeats

AA 237-259 removed in mature form (potential)

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Figure 12

Examples of Trail-R3-Fc fusion proteins with overlapping amino acids
("repeats" included):

Trail-R3 extracellular domain	huIgG1
201 236 SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA	99 120 EP KSCDKTHTCP PCPAPELLGG
SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTP KSCDKTHTCP PCPAPELLGG	
201 236 SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA	99 120 EP KSCDKTHTCP PCPAPELLGG
SPGTPAPAAE ETMTTSPGTP APAAEETMTT SP KSCDKTHTCP PCPAPELLGG	
201 236 SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA	99 120 EP KSCDKTHTCP PCPAPELLGG
SPGTPAPAAE ETMTTSPGTP APAAEETMTT SCDKTHTCP PCPAPELLGG	
201 236 SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA	99 120 EP KSCDKTHTCP PCPAPELLGG
SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGHTCP PCPAPELLGG	
201 236 SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA	99 120 EP KSCDKTHTCP PCPAPELLGG
SPGTPAPAAE ETMTTSPGTP APAAEETMTT HTCP PCPAPELLGG	
201 236 SPGTPAPAAE ETMTTSPGTP APAAEETMTT SPGTPA	99 120 EP KSCDKTHTCP PCPAPELLGG
SPGTPAPAAE ETMTTSPGTP APAAEETMTT HTCP PCPAPELLGG	

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Figure 13

Examples of Trail-R3-Fc fusion proteins with overlapping amino acids
("repeats" not included):

Trail-R3 extracellular domain	huIgG1
121 161 SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVE T	99 120 EP KSCDKTHTCP PCPAPELLGG
SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVEP KSCDKTHTCP PCPAPELLGG	
121 161 SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVE T	99 120 EP KSCDKTHTCP PCPAPELLGG
SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEP KSCDKTHTCP PCPAPELLGG	
121 161 SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVE T	99 120 EP KSCDKTHTCP PCPAPELLGG
SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EP KSCDKTHTCP PCPAPELLGG	
121 161 SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVE T	99 120 EP KSCDKTHTCP PCPAPELLGG
SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEP KSCDKTHTCP PCPAPELLGG	
121 161 SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVE T	99 120 EP KSCDKTHTCP PCPAPELLGG
SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVE THTCP PCPAPELLGG	
121 161 SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATVE T	99 120 EP KSCDKTHTCP PCPAPELLGG
SPEMCRKCSR CPSGEVQVSN CTSWDDIQCV EEFGANATHTCP PCPAPELLGG	

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Figure 14**7. TRAIL-R4**

>sp|Q9UBN6|T10D_HUMAN Tumor necrosis factor receptor superfamily member 10D precursor (Decoy receptor 2) (DcR2) (TNF-related apoptosis-inducing ligand receptor 4) (TRAIL receptor-4) (TRAIL-R4) (TRAIL receptor with a truncated death domain) - Homo sapiens

```
1 60
MGLWGQSVPT ASSARAGRYP GARTASGTRP WLLDPKILKF VVFIVAVLLP VRVDSATIPR
61 120
QDEVPOQTVA PQQQRRSLKE EECPAGSHRS EYTGACNPCT EGVDTIASN NLPSCLLCTV
121 180
CKSGQTNKSS CTTTRDTVCQ CEKGSFQDNK SPEMCRTCRT GCPRGMVKVS NCTPRSDIKC
181 240
KNESAASSTG KTPAAEETVT TILGMLASPY HYLIIIVVLV IILAVVVGF SCRKKFISYL
241 300
KGICSGGGGG PERVHRVLFR RRSCPSRVPG AEDNARNETL SNRYLQPTQV SEQEIQGQEL
301 360
AELTGVTVES PEEPQRLLEQ AEAEGCQRRR LLVPVNDADS ADISTLLDAS ATLEEGHAKE
361 386
TIQDQLVGSE KLFYEDEAG SATSCL
```

AA 1-55 signal peptide
AA 56-211 extracellular domain (potential)
AA 58-97 CRD1
AA 98-139 CRD2
AA 140-180 CRD3
AA 212-232 transmembrane (potential)
AA 233-386 cytoplasmic (potential)

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Figure 15

Examples of Trail-R4-Fc fusion proteins with overlapping amino acids:

Trail-R4 extracellular domain	huIgG1
171 211 NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASPY H	99 120 EP KSCDKTHTCP PCPAPELLGG
NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLAS KSCDKTHTCP PCPAPELLGG	
171 211 NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASPY H	99 120 EP KSCDKTHTCP PCPAPELLGG
NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLAS KSCDKTHTCP PCPAPELLGG	
171 211 NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASPY H	99 120 EP KSCDKTHTCP PCPAPELLGG
NCTPRSDIKC KNESAASSTG KTPAAEETVT THTCP PCPAPELLGG	
171 211 NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASPY H	99 120 EP KSCDKTHTCP PCPAPELLGG
NCTPRSDIKC KNESAASSTG KTPAAEETVT TILGMLASPY THTCP PCPAPELLGG	

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Figure 16

1. TNF-R1

>sp|P19438|TR1A_HUMAN Tumor necrosis factor receptor superfamily member 1A precursor (p60) (TNF-R1) (TNF-RI) (p55) (CD120a) [Contains: Tumor necrosis factor binding protein 1 (TBPI)] - Homo sapiens (Human).

```

1                                     60
MGLSTVPDLL LPLVLELLV GIYPSGVIGL VPHLG DREKR DSVCPQGKYI HPQNN SICCT
61                                     120
KCHKGTLYLN DCPGPGQDTD CRECESGSFT ASENHLRHCL SCSKCRKEMG QVEISSCTVD
121                                     180
RDTVCGCRKN QYRHYWSENL FQCFNCSLCL NGTVHLSCQE KQNTVCTCHA GFFLRENECV
181                                     240
SCSNCKKSLE CTKLCLPQIE NVKGTEDSGT TVLLPLVIFV GLCLLSLLFI GLMYRYQRWK
241                                     300
SKLYSIVCGK STPEKEGELE GTTTPKPLAPN PSFSPTPGFT PTLGFSPVPS STFTSSSTYT
301                                     360
PGDCPNFAAP RREVAPPYQG ADPILATALA SDPIP NPLQK WEDSAHKPQS LDTDDPATLY
361                                     420
AVVENVPPLR WKEFVRRRLGL SDHEIDRLEL QNGRCLREAQ YSMLATWRRR TPRREATLEL
421                                     455
LGRVLRDMDL LGCLEDIEEA LCGPAALPPA PSLLR

```

AA 1-21 Signal peptide
 AA 22-211 extracellular domain (potential)
 AA 43-82 CRD1
 AA 83-125 CRD2
 AA 126-166 CRD3
 AA 167-196 CRD4
 AA 212-234 transmembrane (potential)
 AA 235-455 cytoplasmic (potential)

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Figure 17

Examples of TNF-R1-Fc fusion proteins with overlapping amino acids:

TNF-R1 extracellular domain		huIgG1	
171	211	99	120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE ¹⁷¹ DSGT T		EP KSCDKTHTCP PCPAPELLGG	
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE ¹⁷¹ EP KSCDKTHTCP PCPAPELLGG			
171	211	99	120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE ¹⁷¹ DSGT T		EP K ⁹⁹ SCDKTHTCP PCPAPELLGG	
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVK ⁹⁹ SCDKTHTCP PCPAPELLGG			
171	211	99	120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE ¹⁷¹ DSGT T		EP K ⁹⁹ SCDK ⁹⁹ THTCP PCPAPELLGG	
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVK ⁹⁹ THTCP PCPAPELLGG			
171	211	99	120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE ¹⁷¹ DSGT T		EP K ⁹⁹ SCDK ⁹⁹ THTCP PCPAPELLGG	
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE ¹⁷¹ SCDKTHTCP PCPAPELLGG			
171	211	99	120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE ¹⁷¹ DSGT T		EP K ⁹⁹ SCDK ⁹⁹ THTCP PCPAPELLGG	
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE ¹⁷¹ DKTHTCP PCPAPELLGG			
171	211	99	120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE ¹⁷¹ DSGT T		EP K ⁹⁹ SCDK ⁹⁹ THTCP PCPAPELLGG	
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE ¹⁷¹ DSGT THTCP PCPAPELLGG			
171	211	99	120
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE ¹⁷¹ DSGT T		EP K ⁹⁹ SCDK ⁹⁹ THTCP PCPAPELLGG	
GFFLRENECV SCSNCKKSLE CTKLCLPQIE NVKGTE ¹⁷¹ DSGTHTCP PCPAPELLGG			

Figure 18**2. TNF-R2**

>sp|P20333|TR1B_HUMAN Tumor necrosis factor receptor superfamily member 1B precursor (Tumor necrosis factor receptor 2) (p80) (TNF-R2) (p75) (CD120b) (Etanercept) [Contains: Tumor necrosis factor binding protein 2 (TBPII)] - Homo sapiens (Human).

```
1 60
MAPVAVWAAL AVGLELWAAA HALPAQVAFT PYAPEPGSTC RLREYYDQTA QMCCSKCSPG
61 120
QHAKVFCTKT SDTVCDSCED STYTQLWNWV PECLSCGSRG SSDQVETQAC TREQNRITC
121 180
RPGWYCALSQ QEGCRLCAPL RKCRPGFGVA RPGTETSDVV CKPCAPGTFS NTTSSDTCR
181 240
PHQICNVVAI PGNASMDAVC TSTSPTRSMA PGAVHLPOPV STRSQHTQPT PEPSTAPSTS
241 300
FLLPMGSPSP AEGSTGDFAL PVGLIVGVTG LGLLIIGVVN CVIMTQVKKK PLCLQREAKV
301 360
PHLPADKARG TQGPEQQHLL ITAPSSSSSS LESSASALDR RAPTRNQPQA PGVEASGAGE
361 420
ARASTGSSDS SPGGHGTQVN VTCIVNVCSS SDHSSQCSSQ ASSTMGDTDS SPSESPKDEQ
421 461
VPFSKEECAP RSQLETPETL LGSTEEKPLP LGVPDAGMKP S
```

AA 1-22 Signal peptide
AA 23-257 extracellular domain (potential)
AA 39-76 CRD1
AA 77-118 CRD2
AA 119-162 CRD3
AA 163-201 CRD4
AA 258-287 transmembrane (potential)
AA 288-461 cytoplasmic (potential)

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Figure 19

Examples of TNF-R2-Fc fusion proteins with overlapping amino acids:

TNF-R2 extracellular domain		huIgG1	
221	257	99	120
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		EP KSCDKTHTCP PCPAPELLGG	
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEP KSCDKTHTCP PCPAPELLGG			
221	257	99	120
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		EP KSCDKTHTCP PCPAPELLGG	
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP KSCDKTHTCP PCPAPELLGG			
221	257	99	120
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		EP KSCDKTHTCP PCPAPELLGG	
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP KSCDKTHTCP PCPAPELLGG			
221	257	99	120
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		EP KSCDKTHTCP PCPAPELLGG	
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGKSCDKTHTCP PCPAPELLGG			
221	257	99	120
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		EP KSCDKTHTCP PCPAPELLGG	
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP KSCDKTHTCP PCPAPELLGG			
221	257	99	120
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		EP KSCDKTHTCP PCPAPELLGG	
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTGDKTHTCP PCPAPELLGG			
221	257	99	120
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTGD		EP KSCDKTHTCP PCPAPELLGG	
STRSQHTQPT PEPSTAPSTS FLLPMGPSPP AEGSTHTCP PCPAPELLGG			